The amendments to claim 1 are supported by the claims as originally filed, and by originally filed claim 15. Support for reciting that R4 cannot be an N-terminal Tyr resiude is supported by the specification as filed, for example page 15 lines 17-18, which recite A(1-4) as a preferred embodiment, which has a C-terminal Tyr residue, and page 15 lines 22-23, which discusses AII (4-8), which did not work and that contains an N-terminal Tyr residue. All other amendments are supported by the claims and specification as originally filed, and thus do not constitute new matter. New claims 35-47 are supported by originally filed claim 19, and thus do not constitute new matter.

REMARKS

Objections to the Specification

The Examiner objected to the specification based on the assertion that the use of brackets in the text was misleading, since brackets are sometimes used to indicate amendments to the claims. The Applicants traverse this rejection, as it is clear that the specification as filed would not contain such amendments in the specification. Furthermore, the Examiner has cited no authority for the proposition that the use of brackets in the specification is inherently confusing and is therefore not permissible. However, solely in order to expedite prosecution of the application, the Applicants have amended the specification as requested by the Examiner. This amendment in no way serves as a limitation on the scope of any claims pursued in the present application. Thus, the Applicants respectfully request withdrawal of this objection.

Rejection for obviousness-type double patenting

The Examiner provisionally rejected claims 1-29 for obviousness-type double patenting, based on the assertion that they were not patentably distinct from claims in the 09/307,940

application. The Applicants acknowledge the rejection, and will address the issue when the claims are otherwise allowable.

Claim rejections under 35 USC 112 second paragraph

a) The Examiner rejected claims 1-34 as being indefinite for containing non-elected sequences. Specifically, the Examiner has asserted that claim 1 includes non-elected sequences and that claims 2-34 are rejected based on their dependency on claim 1 and that they do not correct the deficiency of claim 1. The Applicants traverse this rejection. Claims 2-6, 11, 13, and 15-18 have been canceled, obviating their rejection.

As an initial matter, the Applicants note that claim 14 limits the active agent of claim 1 to an active agent comprising a sequence consisting of SEQ ID NO:4, the elected species. Thus, the Examiner's assertion with respect to claims 14 is clearly incorrect.

Claims 1 and 7-10 are generic claims that encompass the elected species. According to 37 CFR 1.146, "in the first action on an application containing a generic claim to a generic invention (genus) and claims to more than one patentably distinct species embraced thereby, the examiner may require the applicant in the reply to that action to elect a species of his or her invention to which his or her claim will be restricted **if no claim to the genus is found to be allowable**." Thus, the patent rules recognize that an Applicant may pursue genus claims, even where a species election is made. Furthermore, the genus recited in claim 1 has been substantially narrowed to facilitate searching by the Examiner.

Furthermore, the claims have been amended to remove recitation of species other the elected species. Based on the above, and the claim amendments made herein, the claims are definite, and one of skill in the art would be well aware of the subject matter that the Applicants

regard as the invention. Therefore, the Applicants respectfully request reconsideration and withdrawal of this rejection.

b) The Examiner rejected claims 1-27 based on the assertion that they lack essential steps, specifically, the method of administration and the outcome of the treatment. The Applicants traverse this rejection. As recited in the specification on page 22 line 21 to page 24 line 17, there are multiple possible modes of administration, and the Examiner has cited no basis for requiring that the claims be limited to a specific mode of administration. Furthermore, claims 22-25 all recite a specific mode of administration.

With respect to "the outcome of treatment", claim 1, on which the remaining claims ultimately depend, recites "An improved method for chemotherapy in a human patient, wherein the improvement comprises administering to the human chemotherapy patient an amount effective for **treating or preventing chemotherapy side effects** of at least one active agent..." Thus, the claims recite a method for treating or preventing chemotherapy side effects. The Examiner has failed to provide any authority for the assertion that some further step must be added in order to make the claims definite.

Thus, the Applicants respectfully request reconsideration and withdrawal of this rejection.

c) The Examiner rejected claims 6-10, 13, 14, and 18 as being indefinite, based on the assertion that the recitation of "consists essentially of" renders the claim indefinite. The Applicants traverse this rejection. However, solely in order to expedite prosecution of the present application, and without prejudice to the refiling of the claims in their original form in a subsequent application, the Applicants have amended the claims to obviate the rejection. Thus, the Applicants respectfully request reconsideration and withdrawal of this rejection.

d) Claims 20, 21, and 28 were rejected as indefinite based on the assertion that the recitation of "between about..." renders the claim indefinite. The Applicants traverse this rejection However, solely in order to expedite prosecution of the present application, and without prejudice to the refiling of the claims in their original form in a subsequent application, the Applicants have amended the claims to obviate the rejection. Thus, the Applicants respectfully request reconsideration and withdrawal of this rejection.

If the Examiner believes that a telephone or personal interview would expedite prosecution of the instant application, the Examiner is invited to call the undersigned at (312) 913-2106.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Date: 11/26/02

By: _____
David S. Harper
Registration No. 42,636

AMENDMENTS

In the Specification:

Please replace the paragraph at page 10 lines 3-15 with the following:

U.S. Patent No. 5,015,629 to DiZerega (the entire disclosure of which is hereby incorporated by reference) describes a method for increasing the rate of healing of wound tissue, comprising the application to such tissue of angiotensin II (AII) in an amount that is sufficient for said increase. The application of AII to wound tissue significantly increases the rate of wound healing, leading to a more rapid re-epithelialization and tissue repair. The term AII refers to an octapeptide present in humans and other species having the sequence Asp-Arg-Val-Tyr-Ile-His-Pro-Phe **(SEQ ID NO:1)** ~~[SEQ ID NO:1]~~. The biological formation of angiotensin is initiated by the action of renin on the plasma substrate angiotensinogen (Clouston et al., *Genomics* 2:240-248 (1988); Kageyama et al, *Biochemistry* 23:3603-3609; Ohkubo et al., *Proc. Natl. Acad. Sci.* 80:2196-2200 (1983); each reference hereby incorporated in its entirety). The substance so formed is a decapeptide called angiotensin I (AI) which is converted to AII by the angiotensin converting enzyme (ACE) which removes the C-terminal His-Leu residues from AI **(SEQ ID NO:37)** ~~[SEQ ID NO:37]~~. AII is a known pressor agent and is commercially available.

Please replace the text at page 12 lines 11-16 with the following:

A peptide agonist selective for the AT2 receptor (AII has 100 times higher affinity for AT2 than AT1) has been identified. This peptide is p-aminophenylalanine 6-AII ~~[~~ ~~('(p-NH_2-~~ Phe)6-AII")~~]~~, Asp-Arg-Val-Tyr-Ile-Xaa-Pro-Phe **(SEQ ID NO:36)** ~~[SEQ ID NO:36]~~ wherein Xaa is p-NH_2-Phe (Speth and Kim, BBRC 169:997-1006 (1990). This peptide gave binding characteristics comparable to AT2 antagonists in the experimental models tested (Catalioto, et al., *Eur. J. Pharmacol.* 256:93-97 (1994); Bryson, et al., *Eur. J. Pharmacol.* 225:119-127 (1992).

Please replace the text at page 15 lines 12-23 with the following:

Particularly preferred embodiments of this class comprise the following sequences: AII (SEQ ID NO:1), AIII or AII(2-8), Arg-Val-Tyr-Ile-His-Pro-Phe **(SEQ ID NO:2)** ~~[SEQ ID~~ **(SEQ ID NO:3)** ~~[SEQ ID NO:3]~~; AII(1-7), Asp-Arg-Val-Tyr-Ile-His-Pro **(SEQ ID NO:4)** ~~[SEQ ID NO:4]~~; AII(2-7). Arg-Val-Tyr-Ile-His-Pro **(SEQ ID NO:5)** ~~[SEQ ID NO:5]~~; AII(3-7), Val-Tyr-Ile-His-Pro **(SEQ ID NO:6)** ~~[SEQ ID NO:6]~~; AII(5-8), Ile-His-Pro-Phe **(SEQ ID NO:7)** ~~[SEQ ID NO:7]~~; AII(1-6), Asp-Arg-Val-Tyr-Ile-His **(SEQ ID NO:8)** ~~[SEQ ID NO:8]~~; AII(1-5), Asp-Arg-Val-Tyr-Ile **(SEQ ID NO:9)** ~~[SEQ ID NO:9]~~; AII(1-4), Asp-Arg-Val-Tyr **(SEQ ID NO:10)** ~~[SEQ ID NO:10]~~; and AII(1-3), Asp-Arg-Val **(SEQ ID NO:11)** ~~[SEQ ID NO:11]~~. Other preferred embodiments include: Arg-norLeu-Tyr-Ile-His-Pro-Phe**(SEQ ID NO:12)** ~~[SEQ ID NO:12]~~ and Arg-Val-Tyr-norLeu-His-Pro-Phe**(SEQ ID NO:13)** ~~[SEQ ID NO:13]~~. Still another preferred embodiment encompassed within the scope of the invention is a peptide having the sequence Asp-Arg-Pro-Tyr-Ile-His-Pro-Phe **(SEQ ID NO:31)** ~~[SEQ ID NO:31]~~. AII(6-8), His-Pro-Phe **(SEQ ID NO:14)** ~~[SEQ ID NO:14]~~ and AII(4-8), Tyr-Ile-His-Pro-Phe **(SEQ ID NO:15)** ~~[SEQ ID NO:15]~~ were also tested and found not to be effective.

Please replace the text at page 17 lines 1-7 with the following:

A particularly preferred subclass of the compounds of general formula II has the formula

R^2-R^3-Tyr-R^5-His-Pro-Phe**(SEQ ID NO:16)** ~~[SEQ ID NO:16]~~

wherein R^2, R^3 and R^5 are as previously defined. Particularly preferred is angiotensin III of the formula Arg-Val-Tyr-Ile-His-Pro-Phe **(SEQ ID NO:2)** ~~[SEQ ID NO:2]~~. Other preferred compounds include peptides having the structures Arg-Val-Tyr-Gly-His-Pro-Phe **(SEQ ID NO:17)** ~~[SEQ ID NO:17]~~ and Arg-Val-Tyr-Ala-His-Pro-Phe **(SEQ ID NO:18)** ~~[SEQ ID~~

~~NO:18~~]. The fragment AII(4-8) was ineffective in repeated tests; this is believed to be due to the exposed tyrosine on the N-terminus.

In the claims:

Please cancel claims 2-6, 11, 13, and 15-18

Please amend the claims as follows:

1. (Amended) An improved method for chemotherapy in a human patient, wherein the improvement comprises administering to the human chemotherapy patient an amount effective for treating or preventing chemotherapy side effects of at least one active agent comprising a sequence **consisting** of at least three contiguous amino acids of groups R^1-R^8 in the sequence of general formula I

$$R^1\text{-}R^2\text{-}R^3\text{-}R^4\text{-}R^5\text{-}R^6\text{-}R^7\text{-}R^8$$

wherein R^1 is [~~selected from the group consisting of H,~~] Asp [~~, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me^{2}Gly, Pro, Bet, Glu(NH_2), Gly, Asp(NH_2) and Suc~~],

R^2 is [~~selected from the group consisting of~~] Arg **or**[~~, Lys, Ala, Orn, Ser(Ac), Sar,~~] D-Arg [~~and D-Lys~~];

R^3 is selected from the group consisting of Val, [~~Ala,~~] Leu, [~~Lys,~~] **and** norLeu, [~~Ile, Gly, Pro, Aib, Acpc and Tyr~~];

R^4 is selected from the group consisting of Tyr[,] **and** Tyr(PO_3)$_2$ [~~, Thr, Ser, Ala, homoSer and azaTyr~~];

R^5 is [~~selected from the group consisting of~~] Ile[~~, Ala, Leu, norLeu, Val and Gly~~];

R^6 is [~~selected from the group consisting of~~] His[~~, Arg or 6-NH_2-Phe~~];

R^7 is [~~selected from the group consisting of~~] Pro [~~or Ala~~]; and

R^8 is [~~selected from the group consisting of~~] Phe **or is absent**[~~, Phe(Br), Ile and Tyr~~],

excluding sequences including R^4 as a**n N**-terminal Tyr group;

and wherein the active agent is not SEQ ID NO:1.

2. **(Cancel)** [~~The method of claim 1 wherein the active agent comprises a sequence of at least four contiguous amino acids of groups R^1-R^8 in the sequence of general formula I.~~]

3. **(Cancel)** [~~The method of claim 1 wherein the active agent comprises a sequence of at least five contiguous amino acids of groups R^1-R^8 in the sequence of general formula I.~~]

4. **(Cancel)** [~~The method of claim 1 wherein the active agent comprises a sequence of at least six contiguous amino acids of groups R^1-R^8 in the sequence of general formula I.~~]

5. **(Cancel)** [~~The method of claim 1 wherein the active agent comprises a sequence of at least seven contiguous amino acids of groups R^1-R^8 in the sequence of general formula I.~~]

6. **(Cancel)** [~~The method of claim 1 wherein the active agent consists essentially of a sequence of at least three contiguous amino acids of groups R^1-R^8 in the sequence of general formula I.~~]

7. **(Amended)** The method of claim 1 wherein the [~~active agent~~] **sequence** consists [~~essentially of a sequence~~] of at least four contiguous amino acids of groups R^1-R^8 in the sequence of general formula I.

8. **(Amended)** The method of claim 1 wherein the [~~active agent~~] **sequence** consists [~~essentially of a sequence~~] of at least five contiguous amino acids of groups R^1-R^8 in the sequence of general formula I.

9. **(Amended)** The method of claim 1 wherein the [~~active agent~~] **sequence** consists[~~essentially of a sequence~~] of at least six contiguous amino acids of groups R^1-R^8 in the sequence of general formula I.

10. (**Amended**) The method of claim 1 wherein the [~~active agent~~] **sequence** consists [~~essentially of a sequence~~] of at least seven contiguous amino acids of groups R^1-R^8 in the sequence of general formula I.

11. (Canceled) [~~The method of claim 1 wherein the active agent comprises a sequence selected from the group consisting of angiotensinogen, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO: 34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, and SEQ ID NO:42.~~]

12. (Canceled) [~~The method of claim 1 wherein the active agent comprises the amino acid sequence of SEQ ID NO:4.~~]

13. (Canceled) [~~The method of claim 1 wherein the active agent consists essentially of a sequence selected from the group consisting of angiotensinogen, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO: 34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, and SEQ ID NO:42.~~]

14. (Amended) The method of claim 1 wherein the [~~active agent~~] **sequence** consists [~~essentially~~] of the amino acid sequence of SEQ ID NO:4.

15. (Canceled) [~~The method of claim 1 wherein the active agent comprises a sequence of the following general formula II:~~

~~Asp-Arg-R1-R2-Ile-His-Pro-R3, wherein~~

~~R1 is selected from the group consisting of Val, Pro, Lys, Norleu, and Leu;~~

~~R2 is selected from the group consisting of Ala, Tyr, and Tyr$(PO_3)_2$; and~~

~~R3 is Phe or is absent.~~]

16. (Canceled) [~~The method of claim 1 wherein the active agent consists essentially of a sequence of the following general formula II:~~

~~Asp-Arg-R1-R2-Ile-His-Pro-R3, wherein~~

~~R1 is selected from the group consisting of Val, Pro, Lys, Norleu, and Leu;~~

~~R2 is selected from the group consisting of Ala, Tyr, and Tyr$(PO_3)_2$; and~~

~~R3 is Phe or is absent.~~]

17. (Canceled) [~~The method of claim 15 wherein the active agent comprises a sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, and SEQ ID NO:41.~~]

18. (Canceled) [~~The method of claim 16 wherein the active agent consists essentially of a sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, and SEQ ID NO:41~~.

20. (Amended) The method of claim 1 wherein the active agent is administered at a dosage of between [~~about~~] 2.5 μg/kg/day and [~~about~~] 100 μg/kg/day.

21. (Amended) The method of claim 1 wherein the active agent is administered at a dosage of between [~~about~~] 10 μg/kg/day and [~~about~~] 75 μg/kg/day.

28. (Amended) A pharmaceutical composition comprising

a) an amount of the active agent of claim 1 sufficient to provide a dosage to a patient of between [~~about~~] 2.5 μg/kg/day and [~~about~~] 100 μg/kg/day; and

b) a pharmaceutically acceptable carrier.

29. (Amended) The pharmaceutical composition of claim 28 wherein the [active agent] **sequence consists of the amino acid sequence** [~~is selected from the group consisting~~] of SEQ ID NO:4 [~~and SEQ ID NO:41~~].

Please add the following new claims:

35. **(New)** The method of claim 19 wherein the side effect is hematopoietic toxicity.

36. **(New)** The method of claim 19 wherein the side effect is decreased mobilization of hematopoietic progenitor cells from bone marrow into the peripheral blood.

37. **(New)** The method of claim 19 wherein the side effect is anemia.

38. **(New)** The method of claim 19 wherein the side effect is myelosuppression.

39. **(New)** The method of claim 19 wherein the side effect is pancytopenia.

40. **(New)** The method of claim 19 wherein the side effect is thrombocytopenia.

41. **(New)** The method of claim 19 wherein the side effect is neutropenia.

42. **(New)** The method of claim 19 wherein the side effect is lymphopenia.

43. **(New)** The method of claim 19 wherein the side effect is leukopenia.

44. **(New)** The method of claim 19 wherein the side effect is stomatitis.

45. **(New)** The method of claim 19 wherein the side effect is alopecia.

46. **(New)** The method of claim 19 wherein the side effect is headache.

47. **(New)** The method of claim 19 wherein the side effect is muscle pain.